DEPARTMENT OF HEALTH AND HUMAN SERVICES

and

CENTERS FOR DISEASE CONTROL AND PREVENTION

convene the

ADVISORY COUNCIL FOR THE ELIMINATION OF TUBERCULOSIS

Atlanta, Georgia
February 16-17, 2005

RECORD OF THE PROCEEDINGS

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Minutes of the Meeting

The Department of Health and Human Services (HHS) and the Centers for Disease Control and Prevention (CDC) convened a meeting of the Advisory Council for the Elimination of Tuberculosis (ACET). The proceedings were held on February 16-17, 2005 at CDC's Corporate Square Facility, Building 8, in Atlanta, Georgia.

Opening Session

Dr. Masae Kawamura, the ACET Chair, called the meeting to order at 8:35 a.m. on February 16, 2005. She welcomed the attendees to the proceedings and opened the floor for introductions. The following individuals were present for the deliberations.

ACET Members
Dr. Masae Kawamura, Chair
Dr. Michael Fleenor
Dr. Jennifer Flood
Dr. Richard Fluck
Dr. David Gonzales
Ms. Eileen Napolitano

***Ex Officio*s and Liaisons**
Dr. William Baine (AHRQ)
Dr. Henry Blumberg (IDSA)
Dr. Fred Gordin (ATS)
Ms. Eva Moya (U.S.-Mexico BHC)
Ms. Tanya Oemig (NTCA)
Dr. Michael Puisis (NCCHC)
Dr. Lee Reichman (ACCP)
Dr. Gary Roselle (VA)
Dr. Diana Schneider (DIHS)
Ms. Rachel Stricof (APIC)
Dr. Litjen Tan (AMA)
Dr. Michael Tapper (SHEA)
Dr. Nancy Warren (APHL)
Dr. David Weissman (NIOSH)

Designated Federal Official
Dr. Ronald Valdiserri,
Executive Secretary

CDC Representatives
Dr. Janet Collins
(NCHSTP Acting Director)
Dr. Kenneth Castro, DTBE Director
Mr. John Anderson
Dr. Peter Cegielski

Dr. Terence Chorba
Dr. Mitchell Cohen
Ms. Ann Cronin
Ms. Hazel Dean
Ms. Mollie Ergle (Contractor)
Ms. Paulette Ford-Knights
Dr. Victoria Gammino
Ms. Judy Gibson
Dr. Stefan Goldberg
Dr. Garth Graham
Ms. Tina Hill
Mr. Dale Hu
Dr. Michael Iademarco
Ms. Margaret Jackson
Dr. Paul Jensen
Dr. John Jereb
Dr. Dolly Katz
Ms. Sophia Kazamora
Ms. Kimberly Lane
Ms. Ann Lanner
Dr. Kayla Laserson
Mr. Chris McLaughlin
Dr. Adelisa Panlilio
Dr. Phillip Talboy
Dr. Zachary Taylor
Dr. Andrew Vernon

Guests

Dr. Edward Ellis (TB Prevention and Control Program-Canada)
Dr. Ann Ginsberg (TB Alliance)
Dr. Vino Molivani (Emory University)
Ms. Carol Pozsik (NTCA)
Mr. John Seggerson (NCET)

Dr. Ronald Valdiserri, the ACET Executive Secretary, made several announcements. ACET meetings are open to the public and all comments made during the proceedings are a matter of public record. Members should be mindful of potential conflicts of interest identified by the CDC Office of Program Services and recuse themselves from voting or participating in these discussions. Liaisons and *ex officios* are non-voting members, but are welcome to provide input throughout the meeting. The terms of Dr. Jeffrey Douglas, Ms. Teresa Garrett and Ms. Eileen Napolitano will expire in June 2005, but these members will continue to serve until officially replaced.

Overview of the Coordinating Center for Infectious Diseases (CCID)

Ms. Kimberly Lane, the CCID Acting Chief Management Officer, provided an overview of CCID. CDC combined its centers, institutes and offices (CIOs) in May 2004 into four new coordinating centers to coordinate programmatic and scientific activities for disease, disability and injury. The new organizational structure will assist CDC in leveraging its resources to be more flexible in responding to public health threats, emerging issues and chronic health conditions. CCID is the largest of CDC's four coordinating centers with ~3,200 full-time employees, >500 contractors and a $3.8 billion budget. The National Center for HIV, STD and TB Prevention (NCHSTP), National Center for Infectious Diseases (NCID), and National Immunization Program (NIP) are housed in CCID.

Several roles and responsibilities were established for CCID. Areas of synergy will be identified for collaboration within NCHSTP, NCID and NIP as well as across other coordinating centers. Opportunities will be identified to coordinate and integrate programs across CIOs to improve health outcomes. Infectious disease-specific goals will be achieved. Efforts will be made to ensure that science and programs are of the highest quality and meet CDC goals. Leadership, decision-making and management will be provided to CCID programs. Collaborative efforts will be undertaken with the CDC Office of the Director to reduce redundancies in business practices.

Specific roles and responsibilities were also established for the three CCID centers. A foundation will be provided for scientific and programmatic knowledge and expertise. Daily operations of science and prevention programs will be managed. Efforts will be made to account for the quality of scientific and prevention programs. Statutory requirements will be met. CCID's functions include management, enterprise communications, strategy and innovation, science and public health practice, program integration, and workforce and career development. Examples of CCID's functions are outlined as follows. Dr. Mitchell Cohen, the CCID Director, will coordinate CDC's research and program development action plans to achieve health protection goals and will also advise CDC's senior leadership on strategies and policies of relevance to research and program development. The key performance indicator (KPI) of this position will be CCID's annual health protection impact appraisal.

The Chief Management Official will ensure that CCID's management practices are based on the highest standards of quality, equity, integrity and humanitarianism and will also assess and support the performance of CCID's management and administrative team members. The KPI of this position will be CCID's annual financial audit. The Enterprise Communications Liaison will ensure excellent communications to CDC's external and internal customers and will also serve as a liaison to the Office of Enterprise Communication. The KPI of this position will be CCID's goal-directed enterprises and development of communication action plans. The Strategy and Innovation Liaison will measure, report and improve CDC's performance and progress toward achieving its health protection and health equity goals and will also serve as a liaison to the Office of Strategy of Innovation (OSI). The KPI of this position will be CCID's effective participation in CDC's health protection goals and goal management plans.

The Senior Advisor for Science and Public Health Practice will ensure excellent science as the foundation to accomplish CDC's mission, strategies and goals and will also serve on CDC's Excellence in Science Committee and Animal Policy Board. The KPI of this position will be CCID's effective participation in CDC's health protection and goal-directed research agendas and implementation plans. The Workforce and Career Development Liaison will develop and execute CDC's workforce and career

development diversity strategies and policies to support CDC's health protection goals and will also provide advice to the CCID Director on these issues. The KPI of this position will be CCID's effective participation in CDC's goal-directed action plan for workforce and career development diversity improvement.

CCID has identified several priorities that need to be addressed in the near future. A mission and functional statements for the coordinating center and three individual centers will be developed and persons will be recruited to permanently fill positions by August 1, 2005. Position announcements for the NCHSTP, NCID and NIP Directors will close on May 3, 2005 and a search committee is being established. The FY'05 budget will be executed in collaboration with NCHSTP, NCID and NIP. Reviews will be completed of CCID grants and cooperative agreements, the role of CCID field staff, and programs that span multiple divisions within CCID to improve the efficiency and effectiveness of infectious disease programs. The CCID organizational chart was distributed to ACET for review.

Update by the NCHSTP Acting Director

Dr. Janet Collins covered the following areas in her report. One, a new Deputy Director for the Division of TB Elimination (DTBE) was appointed; an Acting Associate Director for Laboratory Sciences was selected; and two NCHSTP staff are temporarily assigned to CCID. Applications will be accepted for the Global AIDS Program (GAP) Director through March 31, 2005 and for the NCHSTP Director through May 3, 2005. Two, the FY'05 budget provides an additional $2.64 million for TB, but the increase to DTBE will actually be ~$1.5 million due to the HHS-wide rescission of 0.8% and taps for evaluation funds and the Small Business Innovative Research Program. Congress encouraged CDC to maximize the percentage of TB control funds made available on a per case basis while ensuring that no state receives less funding than in FY'04. The NCHSTP budget will decrease by $4 million in FY'06 based on the President's request, but the FY'05 and FY'06 TB budgets will be equivalent.

Three, CDC is developing an agency-wide research agenda to establish priorities for both intramural and extramural research. Of the six workgroups that were formed to support this effort, two are focusing on infectious diseases and global activities. The infectious diseases workgroup identified 15-20 priority areas based on public health need, relevance to reducing health disparities, potential for broad impact, and relevance to CDC's mission and health protection goals. Internal input on the infectious disease thematic areas was gathered from DTBE and all other NCHSTP divisions and four invitational meetings will be held in March 2005 to collect external feedback. Several TB organizations have been invited to attend the meeting on March 8, 2005 in Washington, DC. The infectious disease workgroup will provide invited participants with

list of documents to review prior to the meeting. The research agenda will have a public comment period from May 1-June 15, 2005 and will be finalized by June 30, 2005. At this time, the budget, actual implementation and full implications of the research agenda have not been defined.

Four, a *Federal Register* notice was published in December 2004 on the draft "Guidelines for Preventing Transmission of TB in Healthcare Settings." The public comment period closed on February 4, 2005 and CDC received 123 submissions in response to the document. ACET and DTBE were well represented at CDC's Stakeholders' Workshop on Respiratory Protection for Airborne Infectious Agents on November 30-December 1, 2004. NCHSTP is informing HHS and Congressional members about TB reports in Hmong refugees. A conference will be held on March 1, 2005 in Botswana in recognition of the 10th anniversary of the BOTUSA Project.

DTBE Director's Report

Dr. Kenneth Castro covered the following areas in his report. One, the Regional Training and Medical Consultation Center (RTMCC) summit was held in January 2005 with the four successful grantees. The RTMCCs will focus on the need to retain proficiency as the number of TB cases declines by ensuring access to training and education and providing expert medical consultation. The RTMCCs will cover four regions and are located in Newark, New Jersey; San Antonio, Texas; San Francisco, California; and Tallahassee, Florida.

Two, a notice was published in the *Morbidity and Mortality Weekly Report* (*MMWR*) in January 2005 announcing CDC's new national program for rapid genotyping of *Mycobacterium tuberculosis* (*M.tb*) isolates. The genotyping program contracts with laboratories in California and Michigan that will provide results within ten working days. The laboratories will rely on two polymerase chain reaction-based methods. The volume of submissions was the major factor in assigning states to either the California or Michigan laboratory. Three, a recommendation was made during a Department of State (DOS) briefing in January 2005 to halt travel among Hmong refugees until re-screening is conducted. High rates of TB and multidrug-resistant TB (MDR-TB) were recently reported in this population. DTBE is providing assistance to an onsite investigation of a Hmong refugee camp in Thailand.

Four, the World Health Organization (WHO) and Office of the Global AIDS Coordinator convened a meeting in February 2005 to discuss strategies to coordinate activities with the President's Emergency Plan for AIDS Relief (PEPFAR). Five, DTBE conducted an internal review of its TB diagnostics portfolio in February 2005 to identify approaches to take advantage of new opportunities in the absence of new TB dollars. Six, the Federal

TB Task Force (FTBTF) held a meeting to provide a progress report on its activities in response to the Institute of Medicine (IOM) report, *Ending Neglect*. FTBTF requested that ACET place the TB outbreak among Hmong refugees on its agenda as a priority item. Seven, DTBE senior staff held a retreat to review progress and develop future plans.

Eight, the nucleic acid amplification testing (NAAT) workgroup is charged with evaluating the need for changes in the current guidance; assessing the consistency between current recommendations and various CDC documents; identifying the available science base for possible revisions; and drafting revised guidelines if appropriate. The NAAT workgroup is considering six questions to fulfill its charge. Do current guidelines meet the needs of controllers, clinicians and laboratorians? Who is the target audience? Should all TB suspects receive NAAT? Should the guidelines address testing of non-respiratory specimens? Can changes in testing algorithms make NAAT cost effective? What are the usefulness and limitations of cost-effectiveness studies of NAAT?

The NAAT workgroup is using several data sources to address the six issues; plans to distribute current guidelines, CDC statements, recommendations and relevant scientific literature; and will convene a conference call to begin the review and evaluation process. An analysis of the utility and cost effectiveness of NAAT for initial evaluation of TB suspects was completed, but the report is still being developed.

Nine, an evaluation is ongoing of multiple diagnostic procedures for latent TB infection (LTBI) in diverse populations. Cohorts being analyzed are healthcare workers (HCWs) and TB suspects in Japan; visa applicants in Vietnam; Naval recruits; TB suspects; TB outbreaks in nurseries, dialysis centers and day care centers; and high-risk groups of homeless persons, HIV-positive individuals, refugees and drug treatment clients. The first-, second- and third-generation QuantiFERON (QFT) TB tests, Elispot test and MFBA assay are included in the assessment. Performance of these tests is also being analyzed in a cohort involved with an outbreak of non-tuberculous mycobacteria in a nail salon. QFT-Gold has been approved by the Food and Drug Administration (FDA). Guidelines are currently being drafted and should be disseminated to ACET by the end of February 2005 for review.

Ten, the 2004 provisional case counts will be released during World TB Day and will show a national decrease in TB from 2003 to 2004. Surveillance is ongoing for adverse effects related to LTBI drugs. DTBE is providing assistance to the New York City Health Department on its investigation of a TB cluster due to *Mycobacterium bovis.* Eleven, efforts are underway on 16 task orders for Tuberculosis Epidemiologic Studies Consortium (TBESC) projects. To date, four projects have completed data collection,

seven projects are currently gathering data, three projects have undergone an Institutional Review Board (IRB) review, and two projects are developing protocols.

The Tuberculosis Trials Consortium (TBTC) has enrolled 4,000 patients in Study 26 to compare 12 doses of isoniazid (INH) and rifapentine versus nine-month therapy of daily INH among persons with LTBI. Study 27 is a Phase II trial evaluating the role of moxifloxacin in TB and early bactericidal activity. TBTC has almost completed Study 27 and expects to present results to the American Thoracic Society in May 2005. Study 28 will be launched in the near future and will be designed as a Phase II clinical trial to compare the microbiological activity and safety of a regimen with moxifloxacin versus the standard control regimen of INH, rifampin (RIF), pyrazinamide and ethambutol.

TBTC will discontinue one large or two small sites in FY'05 due to budget constraints. Despite funding limitations, however, DTBE is committed to continuing its $9 million infrastructure for TB research. Collaborations between CDC field stations and the National Institutes of Health are being explored to broaden capacity to conduct clinical and health systems research. The potential to expand long-term banking for genetic studies is being considered.

ACET made several comments in response to the CCID, NCHSTP and DTBE updates. CDC is commended for its outstanding efforts to develop a streamlined organizational structure, but concerns have been expressed that local and state health department capacity to conduct TB activities and meet other public health challenges may weaken in the future. For example, CDC's reorganization is the vision of Dr. Julie Gerberding, the CDC Director, but current plans may not be continued if she no longer serves in this position. Several of CDC's senior leadership positions are currently vacant due to retirements. Funding for the daily operation and management of the new coordinating centers and offices will result in smaller allocations to programs. ACET also made specific suggestions to DTBE in response to the updates.

- Ensure that the infectious disease component of the CDC-wide research agenda is informed by existing TB activities, particularly TBESC and TBTC projects.
- Ask CCID to address a cross-cutting issue among NCHSTP, NCID and NIP. For example, TB control, infectious disease and immunization programs that receive CDC dollars will be tremendously impacted if block grants are actually eliminated from the FY'06 President's budget.
- Re-shift priorities to include the evaluation of multiple diagnostic procedures for LTBI in high-risk populations as a formal TBESC study.

CDC made follow-up remarks to ACET's discussion. Dr. Gerberding has leveraged strong support from all levels of CDC and Congress to implement the new

organizational structure. CDC is also concerned about the large number of vacancies of key leadership positions, but a solid workforce and career development plan will be designed to more strongly focus on succession planning. A workforce evaluation is currently being conducted of public health advisors assigned to state and local health departments since the majority of these personnel will be eligible for retirement over the next ten years. This analysis will result in recommendations to ensure that capacity in the field does not decrease.

CDC's FY'05 budget includes a new line item for leadership and management support in which 10% of overhead funding or ~$10 million will be withheld and allocated to programs as an incentive to implement goals management activities. FY'05 funding for programs is intact compared to FY'04. Coordinating centers cannot use program funds for daily operation and management. Instead, the CDC Office of the Director will allocate dollars to coordinating centers for overhead expenses. Programs will continue to operate at the level of divisions.

Global TB Epidemiology Report

Dr. Victoria Gammino of DTBE provided an overview of the epidemiology of global TB. Of the world population, 33% is infected with TB. The disease kills one person every 17 seconds, resulting in >2 million deaths each year. Of all TB deaths, 98% live in developing countries. Of the 9 million new TB cases reported in 2002, 80% were in 22 high-burden countries (HBCs). MDR-TB continues to threaten TB control and TB/HIV co-infection is a growing syndemic. Of TB cases in the United States, 53% are among foreign-born persons. A 2003 WHO report showed that TB was one of the top five leading causes of mortality from infectious diseases. The annual number of deaths worldwide from TB is estimated to be 1.6 million, but an additional 15% of 2.9 million AIDS deaths attributable to TB are not captured in official TB mortality figures.

A downward trend in TB incidence has been seen in several regions of the world since the 1980s, but African and some ex-Soviet countries have demonstrated an upward trend. A WHO 2004 report showed that India and China had the highest estimated incidence of TB in 2002. The preponderance of countries with TB incidence rates >100/100,000 is concentrated in Africa and Asia, while countries with incidence rates >300/100,000 are primarily found in sub-Saharan Africa. UNAIDS estimates that ~7.4 million persons are living with HIV/AIDS in Asia. An estimated 5.1 million persons living with HIV/AIDS in India represent the largest number of individuals with the infection outside of Africa.

Increasingly high rates of HIV have played a significant role in global TB epidemiology. In Botswana, Cote d'Ivoire, Malawi, Tanzania and Zimbabwe, rates of TB have

drastically increased since 1980. Studies have shown that 50%-90% of hospitalized TB patients in Botswana are co-infected with HIV. In Uganda, TB case rates continue to rise despite a decline in HIV incidence owing to the large pool of individuals living with HIV/AIDS. MDR-TB continues to be a significant threat to global TB control. Where MDR-TB is a problem, traditional short-course therapy is rendered ineffective due to high rates of resistance to the two most effective drugs, INH and RIF. The danger of drug resistance is especially important given the slowness of the drug development pipeline. TB rates have declined in the United States since 1992 to a low rate of 5.1/100,000 in 2003. However, the proportion of TB cases in foreign-born persons has steadily increased since the mid-1980s. Foreign-born TB cases represented >53% of TB cases in the United States in 2003.

In 2003, 72% of 90 reported primary MDR-TB cases were among foreign-born persons. In 2003, 26% of foreign-born TB cases reported in the United States were from Mexico. TB clusters and outbreaks among foreign-born persons pose serious challenge to TB control efforts in the United States due to difficulties in accessing populations, language barriers and cultural beliefs.

The internationally recommended TB control strategy is directly observed treatment short-course (DOTS) and calls for the national case management of populations. In 1997, the World Health Assembly declared that DOTS represents the most important public health breakthrough of the decade in terms of saving lives. The five essential elements of the DOTS strategy are: government commitment to TB control; microscopy-based case detection; standardized short-course chemotherapy under DOT; a secure supply of quality drugs; and case registry, monitoring and evaluation.

Several epidemiological studies have demonstrated the effectiveness of DOTS. DOTS resulted in a 48% reduction in the prevalence of pulmonary TB in China in 1990-2000 compared to a 16% reduction in non-DOTS regions; a treatment success rate of 71% in the first year of implementation in Leningrad; cure rates of ~80% in India; and prevention of further spread of drug resistance in Botswana. In 2001, 11 HBCs met or exceeded 80% of treatment success rates. Of 210 countries around the world, 180 are currently implementing DOTS and WHO estimates that 69% of the world population had access to DOTS in 2003. All 22 HBCs have adopted DOTS and Vietnam is the first HBC that met WHO targets for case detection and treatment success.

In 2000, WHO estimated that DOTS programs worldwide would need to increase the number of additional patients enrolled annually by 2.5 to meet the 70% target for case detection by the end of 2005. However, a new target date will be established in 2005 because WHO's 2004 annual report indicates that the targets projected in 2000 will most likely be unmet. WHO identified the six most common constraints among HBCs in global TB control as lack of qualified staff, poor monitoring and evaluation, inadequate

infrastructure, weak laboratories, poor involvement by private and public providers outside of the National TB Program (NTP), and minimal commitment to and capacity for DOTS in peripheral health services. Additional barriers to global TB control include: minimal access to/limitations of DOTS, increasing TB/HIV co-infection, MDR-TB, and insufficient funds.

Several mechanisms are available to address the challenges and barriers to global TB control. The Stop TB Partnership is a global framework of technical, governmental and donor agencies that was established in 2001 to control the TB epidemic and has since gained significant momentum. The organizational structure of the Stop TB Partnership includes a global drug facility, coordinating board, advisory group, and seven workgroups for research, programmatic issues or advocacy/communications. An enhanced DOTS strategy is emerging and will incorporate strategies for TB/HIV co-infection, MDR-TB, and TB control between private and public sectors. PEPFAR is a five-year and $15 billion initiative to combat the global AIDS crisis. DTBE provides technical support to eight of the 15 PEPFAR countries as well as to four GAP countries.

WHO provides significant leadership to TB/HIV co-infection activities by sponsoring workshops, producing written policy and guidelines, and developing comprehensive training materials. The United States is involved in global TB control through partnerships with several federal agencies and non-governmental organizations (NGOs). The Tuberculosis Coalition for Technical Assistance (TBCTA) is a six-member panel of expert TB organizations funded by USAID. This group provides access to technical experts and assistance for U.S. Agency for International Development (USAID) country missions requesting in-country support for TB. USAID established TBCTA for missions to program TB funds through a user-friendly mechanism; it has extended TBCTA funding through 2006. CDC has considerable experience, leadership and expertise in TB, MDR-TB and TB/HIV co-infection; the ability to broker financial and human resources; and a sustained commitment to build capacity.

CDC Response to the IOM Report Global Recommendations

Dr. Castro noted that the IOM report, *Ending Neglect*, contained five recommendations for TB control and elimination. Control should be maintained to eliminate TB, particularly in an era of changing epidemiology. The rate of decline should be accelerated. Efforts should be made to become involved in global TB activities, particularly since TB in foreign-born persons directly affects the United States. Support should be mobilized and new tools should be developed. With the exception of TB components in GAP and PEPFAR for HIV treatment and care, CDC does not receive funding for global TB initiatives. As a result, CDC heavily relies on partnerships to contribute technical support and capacity building for global TB efforts. Most notably,

USAID has allocated ~$90 million to TB in different parts of the world from its funding for emerging and reemerging infectious diseases.

CDC has taken several actions in response to the IOM recommendation to mobilize support. CDC is one of the founding partners of the Stop TB Partnership and provides expertise in the areas of DOTS expansion, TB/HIV co-infection, DOTS-Plus for MDR-TB, new diagnostics and TB vaccine research. To strengthen laboratory capacity, the Stop TB Partnership is implementing both culture and drug susceptibility testing in countries that exclusively relied on smear microscopy. However, this approach continues to face resistance at the global level.

CDC targets TB prevention and control activities to foreign-born persons in the United States. Assistance is provided to WHO to improve TB control and increase access to DOTS in the 22 HBCs. A partnership was established with the Mexico government to develop the U.S. Border binational card. Several TBESC initiatives are attempting to better define the epidemiologic profile of foreign-born persons and create more effective interventions. Activities are underway to improve medical screening and follow-up of TB-positive immigrants and refugees prior to U.S. entry. The possibility of using medical screening of immigrants and refugees as a mechanism to strengthen laboratory infrastructure in country for all TB-positive persons is being explored.

CDC formed a partnership with the U.S. Immigration and Customs Enforcement (ICE) to improve TB detection and follow-up of ICE detainees until therapy is completed. In the area of TB/HIV co-infection, CDC is strongly focusing on efforts to provide anti-retroviral drugs to persons with HIV. A clinical trial is being launched in Botswana to evaluate six-month treatment for LTBI for three years. CDC will use findings from the clinical trial to develop optimal recommendations for the use of LTBI treatment in populations with high rates of TB re-infection.

Global Report on MDR-TB

Dr. Peter Cegielski of DTBE described efforts that are being made to control global MDR-TB. MDR-TB poses a serious threat to TB control in many countries. WHO and the International Union Against Tuberculosis and Lung Disease led the development of the Global Project on Anti-TB Drug Resistance Surveillance in 1994 in response to MDR-TB outbreaks in Europe and the United States in the 1980s-1990s. The project was designed with three major components. An adequate representative sample was taken of all TB patients to obtain precise estimates of the prevalence of MDR-TB. A distinction was made between new and previously treated cases. Drug susceptibility test results of four first-line drugs were collected from quality-assured laboratories using standardized methods. The project resulted in the development of the Supranational

Reference Laboratory Network with ~20-24 laboratories that regularly provide proficiency testing and continuous quality improvement.

Three global drug resistance surveys have been published to date. The 1994-1996 survey included 35 geographic settings and ~50,000 patients tested for drug susceptibility. It statistically represented 16% of reported sputum smear-positive TB cases in the world and ~20% of the global population. The 1996-1999 survey included 72 geographic settings and >68,000 patients. It represented 28% of reported sputum smear-positive TB cases in the world and ~33% of the global population. The 1999-2002 survey included 109 geographic settings and >64,000 patients. It represented 39% of reported sputum smear-positive TB cases in the world. Based on results from all three surveys, resistance to one or more of four anti-TB drugs was detected in nearly 13% of 77,175 new cases and 33% of 12,905 previously treated cases. Full drug susceptibility was seen in 87% of new cases and 67% of previously treated cases.

Resistance to INH and to streptomycin was the most common. Among new patients with any drug resistance, ~60% were resistant to INH or streptomycin and ~20% were resistant to RIF. More resistance to INH, RIF and ethambutol was seen in previously treated cases. MDR-TB was seen in 2.3% of new cases and 16% of previously treated cases. An extremely small fraction of MDR-TB cases had resistance to only INH and RIF because the large majority had resistance to three or four drugs. Similar resistance was seen in previously treated cases. Among drug-resistant cases, MDR-TB accounted for nearly 18% in new cases and nearly 50% in previously treated cases. Serious resistance to drugs other than those for TB was also seen in both new and previously treated cases.

In 2000, the highest prevalence of MDR-TB was seen in Eastern Europe, countries of the former Soviet Union and Asia. In 1999-2002, countries or regions with a combined MDR-TB prevalence of >10% included Central Asian Republics, Baltic Republics, several parts of Russia, Israel and provinces of China. The DOTS strategy alone has not been found to be sufficient in regions with a high prevalence of drug resistance. Based on the global drug resistance surveys and other country data collected by WHO in 2000, the number of MDR-TB cases in newly diagnosed TB patients was estimated to be 273,000. However, the actual incidence is substantially higher because the estimate does not include patients with previous treatment or patients in whom MDR-TB develops during treatment. The former Soviet Republics, Eastern Europe and Asia account for a large majority of the MDR-TB burden in terms of incident cases. Of new MDR-TB cases each year, China and India each report >50,000 and the former Soviet countries report 10,000-50,000.

Anti-TB drug resistance patterns are predicted by the misuse of drugs over time. These trends are also influenced by the dates drugs were first used in humans; the penetration

of drugs into the local marketplace depending on changes in cost, regulatory approval and local drug production; evolution of NTP regimens; and the introduction of free-of-charge treatment by NTP. WHO determined that second-line drugs are widely available in some parts of the world. Previous NTP treatment recommendations were extremely contentious because these strategies added a single drug to a regimen for previously treated patients. As a result, WHO's category 2 treatment regimen for re-treatment of patients with treatment failures, relapses or defaults may not be appropriate.

The Green Light Committee (GLC) was established to review applications from programs interested in purchasing drugs at a reduced cost. GLC also provides technical assistance to help programs strengthen diagnosis and treatment standards to meet international guidelines. GLC reviews a program's culture and drug susceptibility testing ability, other laboratory capacity, assurances to treatment adherence and previous DOTS performance. Laboratory capacity and rapid diagnosis continue to be serious obstacles within programs and human professional capacity must be strengthened to control MDR-TB.

After approving an application, GLC continues to monitor, evaluate and advise the program to improve clinical and programmatic use of drugs and create a broad evidence base for policy development. A two- to four-member GLC team of a microbiologist, clinician and program expert visits programs semiannually or annually to ensure adherence to the protocol that was proposed and approved. Each program is evaluated on its proper administration of DOTS, provision of a safe environment for HCWs, quality of laboratory results and information systems, drug resistance monitoring, and patient enrollment, management and outcomes. Programs also send periodic reports to GLC between site visits.

GLC and WHO strongly urge applicants to develop stringent regulations regarding the importation and quality of drugs, but this issue continues to be a tremendous political barrier because the country's perspective is that the restriction will limit access to life-saving drugs. To date, GLC has held 28 meetings, reviewed >50 applications, approved 25 applications and is currently reviewing eight applications. GLC's activities have resulted in the treatment of >10,000 MDR-TB patients. Aggregate results of five DOTS-Plus pilot projects are expected to be published in *JAMA* in June or July 2005. A database of $\geq$2,200 MDR-TB cases is being developed based on individual data from the pilot projects.

Several mechanisms are available to apply global recommendations to strengthen MDR-TB detection, prevention and treatment. The DOTS-Plus pilot projects have demonstrated feasibility to treat MDR-TB with second-line drugs in less affluent settings. The Global Fund provides programs with financial support to purchase second-line

drugs, laboratory equipment and supplies, and training, infection control measures and social support to TB patients.

In 2004, WHO formally endorsed a policy that a second-line drug regimen was appropriate for patients with MDR-TB or those for whom treatment previously failed. In addition, the WHO Executive Board passed a resolution that explicitly urged the WHO Director General to address MDR-TB and called for appropriate treatment of all TB patients in addition to sputum smear-positive new patients. The resolution will be presented to and discussed by the World Health Assembly in the summer of 2005. Efforts are shifting from pilot projects to the DOTS-Plus expansion phase. Based on preliminary data from the pilot projects, WHO is revising its guidelines for management of MDR-TB globally and intensifying training opportunities for DOTS-Plus and MDR-TB.

ACET made several comments about the three global reports. Most notably, ACET expressed concern about the lack of attention given to Mexico in global TB efforts. Mexico is not included in the Stop TB Partnership and is not listed as one of the 22 HBCs. However, Mexico was responsible for 26% of TB cases among foreign-born persons in the United States in 2003. Bureaucratic issues have delayed the release of USAID funds to Mexico and resulted in limited treatment, care and follow-up of TB patients. These problems have led to minimal funding of the binational TB case management project and a decrease in Mexico's ability to sustain the initiative.

CDC made several remarks in response to ACET's concerns. CDC is closely collaborating with the Mexico National TB Program to ensure that any individual diagnosed with TB on either side of the Border receives appropriate treatment. One of the features of the U.S.-Mexico binational card project is a toll-free telephone number for persons to obtain information on continuing TB care. CDC has also partnered with Mexico in administering surveys to assess the level of drug resistance. Findings from the project will be used to develop treatment guidelines. Mexico was approved as a GLC project in four states and is receiving low-cost second-line drugs for drug-resistant management. CDC hopes that bureaucratic issues will soon be resolved in order for USAID funds to be released to Mexico in support of several new global projects, including operations research of the TB program.

Overview of the Global Alliance for TB Drug Development (GATDD)

Dr. Ann Ginsberg provided a status report on GATDD's recent activities. GATDD is an independent and international NGO that was established in 2000 to stimulate new TB drug development by integrating pharmaceutical expertise and the public health goal of developing new TB drugs. GATDD is supported by funding from U.S. and foreign governments, USAID and private organizations. GATDD was formed with several goals

and strategic objectives. New and better TB drugs will be developed. TB drug development activities will be coordinated and catalyzed worldwide. Affordability, adoption of and access to TB drugs will be ensured. New drugs will be developed to shorten or simplify treatment of active or drug-susceptible TB and also to improve treatment of MDR-TB, TB/HIV co-infection and LTBI.

GATDD established a near-term vision to shorten TB treatment from six months to two to three months and simplify therapy from a daily to weekly course. This strategy will reduce the current regimen of 100-180 doses to eight to 12 doses. GATDD believes this goal is feasible based on several factors. Treatment has already been significantly shortened from 24 months to the current six-month short-course and this experience can be applied to further shorten treatment. Preclinical animal models of TB are still empiric and not fully validated, but the data show reasonable predictive ability. Clinical trials in this effort contain an achievable number of patients.

Evidence has demonstrated that $\geq$80% of patients are most likely cured with only three months of treatment using current standard TB drugs. Preclinical trials have shown that drugs can be developed with longer half-lives and would be suitable for weekly therapy. Strategies are currently available to modify formulations and delivery methods to provide extended activity of drugs. GATDD's long-term vision is to create a TB treatment course of two weeks or less, but this goal will be difficult to achieve without validated models or advances in understanding the biology of persistence.

HHS is a significant contributor to GATDD's success and achievements and is represented on GATDD's board of directors, stakeholder's association and advisory committees. HHS also played an important role in creating GATDD's scientific blueprint and economics report for TB drug development. A number of flexible mechanisms are available for GATDD to conduct projects. For example, GATDD can leverage sponsors, collaborate with partners, serve as a co-developer or investor of compounds, obtain worldwide exclusive royalty-free rights from a manufacturer to develop a TB drug, and outsource activities to contract research organizations.

GATDD is also involved in non-research initiatives. Non-compound projects are being supported to improve the TB drug development landscape. Assistance is being provided to build clinical trials capacity and ensure compounds are adequate at the clinical testing stage. Databases and search engines are being designed to support the development of predictive models. GATDD has built a robust portfolio and currently has multiple projects in the discovery, preclinical or clinical testing phases. Most notably, the moxifloxacin study is being implemented because preclinical data suggest the drug may shorten TB treatment by as much as two months. Moxifloxacin is an approved drug with an excellent safety record in humans and GATDD has leveraged a

pharmaceutical partner to ensure the drug is affordable to endemic countries and sufficient quantities are available.

Several moxifloxacin studies are ongoing, such as two Phase II studies substituting moxifloxacin for ethambutol; a study of fluoroquinolone early bactericidal activity; and a small sub-study of moxifloxacin. TBTC Study 28 and other Phase II studies are being planned, but a dedicated and focused effort is needed to register moxifloxacin to shorten TB treatment while ensuring affordability, access and adoption. In October 2004, GATDD and its pharmaceutical partner held a joint meeting with key stakeholders and experts to formulate a development plan. A follow-up meeting will be convened with sponsors and investigators in March 2005 to complete harmonization, ensure coordination of the Phase II database and protocols, and finalize roles and responsibilities. CDC's TBTC Study 27 has nearly completed enrollment for the moxifloxacin study and FDA has enrolled 25 patients in the study in Brazil.

GATDD must adhere to certain regulations for the moxifloxacin trial because the study is a regulatory submission. Assurances must be made for all study sites to be compliant with good clinical and laboratory practices as established by FDA. Efforts must be made to ensure that the maximum six-month enrollment goal can be met for each study. Two additional Phase II studies must be successfully initiated and two ongoing studies must be completed. Meetings with regulatory agencies will continue to be held. A plan will be developed to evaluate moxifloxacin for MDR-TB treatment.

Moxifloxacin will be registered to shorten TB treatment and collaborative efforts will be undertaken with appropriate partners to accomplish these goals. GATDD recognizes the key contributions of HHS in moxifloxacin clinical development, preclinical support of the PA-824 project and the development of the next generation of nitroimidazoles. Based on these efforts, GATDD sees a bright future for TB drug development. Up to seven compounds may be in the clinical testing phase for TB indication by the end of 2005.

ACET was extremely impressed by GATDD's TB drug development projects. GATDD's tremendous progress and solid partnerships in both public and private sectors are outstanding, particularly since the organization was only established in 2000. ACET requested that GATDD provide an update on the moxifloxacin trial at a future meeting.

Update on TBESC Task Order 9

Dr. Dolly Katz of DTBE explained that in 2002, foreign-born persons in the United States accounted for 51% of TB cases for the first time. TB rates among foreign-born persons have not declined as rapidly as those in U.S.-born persons. TB rates among

foreign-born persons were nearly nine-fold higher than in U.S.-born persons in 2003. Opportunities are being missed to prevent TB in foreign-born persons because the epidemiology of the disease in this population is not understood. To address these issues, DTBE developed Task Order 9 as a prospective and population-based study using 21 TBESC sites and two additional sites. The enhanced surveillance project is designed to evaluate the epidemiology of TB in foreign-born persons and identify missed opportunities for TB prevention in this population.

A sample of 1,500 newly diagnosed TB cases in foreign-born persons will include all cases from small sites, a random sample from large sites, all foreign-born children <5 years of age, all U.S.-born children <5 years of age with at least one foreign-born parent, and all identified source cases. The pilot study of the project included 94 adults, 13 children and adolescents, a 66% participation rate from 21 sites, and mean lengths of interviews of 56 minutes with no interpreter and 74 minutes with an interpreter. Informed consent forms for both adult and pediatric populations were translated into ten languages in addition to English.

The pilot was implemented with three components. In-person interviews were conducted with a survey that asked questions about visa or immigration status and history, sociodemographics, TB symptoms, care-seeking behaviors, patient delays, previous testing and treatment, and knowledge, attitudes and beliefs about TB. The names of participants were matched to the CDC Division of Global Migration and Quarantine (DGMQ) files to obtain results of TB screening tests at U.S. entry. Data were abstracted from standard TB report forms filed in the United States and Canada. Individuals were given $30 to participate in the pilot in the form of cash, grocery coupons, telephone cards or other incentives.

Results from the 94 adult participants in the pilot study are as follows. Of the interviews, 39% were in English, 26% were with a bilingual interviewer and 35% were with an interpreter. The majority of interviews were in English and Spanish. The study participants represented countries throughout the world, but most were from Mexico and Central America. Of the 94 study participants, 57 were males, 37 were females, 28% had an education of eighth grade or less, 56% had an education of high school graduation or above, 29% were immigrants, 21% were U.S. or Canadian citizens, and 11% refused to provided their visa status.

In the 12 months prior to TB diagnosis, 17% of participants reported no symptoms and $\geq$41% reported coughs with blood, weight loss, night sweats or chest pain. Of 65 respondents who reported dates between onset of symptoms and TB diagnosis, the mean time was six months. Of all 94 participants, 83% reported symptoms and 70% of these persons sought care from a physician, self-treatment or non-traditional sources. Of 93 participants, 42% reported receiving the BCG vaccine.

DTBE reached several conclusions based on the pilot project. Foreign-born persons from a wide variety of backgrounds and countries will participate in the study. Participants can provide useful information and the majority will answer questions about their visa status and other sensitive issues. The pilot project also resulted in several accomplishments for DTBE. Local infrastructures were established and 43% of sites used a central IRB. Logistical issues related to interviews were resolved and questionnaires were tested and improved. Internal consistency of responses was demonstrated and a process was drafted to match DGMQ procedures.

Update on Ten Against Tuberculosis (TATB)

Ms. Eva Moya, the ACET liaison to the U.S.-Mexico Border Health Commission (BHC), provided a status report on TATB activities. The ten U.S. and Mexico Border states created TATB in 1995 to address TB as a Border-wide binational public health issue and to facilitate efforts to more effectively focus on TB morbidity, mortality and transmission. TATB is organized with steering and technical committees that include government representatives, stakeholders and NGOs from both the United States and Mexico. Discussions are currently being held for an ACET member to serve as a liaison to TATB.

In November 2002, TATB was officially designated as the technical advisory group of BHC. This collaboration will allow Mexico and the United States to integrate expertise, provide guidance to an international organization, and contribute to the "Border 2012 Environmental Health Program." TATB developed a strategic plan with goals and measurable objectives to guide activities and investments in TB control along the U.S.-Mexico Border toward achieving *Healthy Border 2010* goals. Most notably, TB incidence will be reduced by 10% on the Mexico side of the Border and by 50% on the U.S. side of the Border. The TATB strategic plan has not yet been implemented into actual practice, but is currently being used by state health officers of the ten U.S. and Mexico Border states to strengthen planning, budgetary and strategic activities to manage TB.

The TATB strategic plan goals will be achieved with the following objectives. TB epidemiology, surveillance and case finding will be enhanced. Laboratory infrastructure will be strengthened to enhance TB identification and confirmation. Health promotion, training and communication for TB awareness will be increased. TB case management will be improved. TATB has been holding regional meetings since November 2004 in both the United States and Mexico to obtain input from local communities on the strategic plan. Feedback from the regional meetings will be posted on the BHC web site by March 15, 2005. TATB has also formed a partnership with Rotary International

Clubs to address TB prevention, education and care as well as other health issues related to migration from Mexico to the United States.

TATB is influencing BHC's stronger focus on TB. TATB engaged local communities in TB screening in support of BHC's "Border Binational Health Week" in October 2004. TATB developed a case management proposal recommending that BHC advocate for legislation to expand Medicaid coverage to include undocumented persons. BHC will convene TB controllers and leaders of the U.S.-Mexico Border region in a binational event and will launch an educational flip chart for TB patients. BHC is exploring the possibility of increasing its involvement in the Arizona "Meet and Greet Project" and encouraging the remainder of the U.S.-Mexico Border region to develop a similar model. Under this initiative, ICE detainees who are deported prior to completion of TB treatment are greeted at the Border by a Mexican health authority who will take responsibility for the patient's care.

The BHC web page has been revised to include a section on the importance of TB. ACET and other groups are invited to post important and relevant topics on the site. BHC will participate in the World Health Day theme of "Stop Tuberculosis." BHC is extremely pleased that its partnership with TATB has resulted in a stronger focus on TB, but is also concerned about recent actions taken by two states. California has recommended that funding for the state Office of Border Binational Health be eliminated and Arizona passed a proposition to limit certain services to persons who cannot prove legal U.S. citizenship.

Update on International Workgroup Activities

Dr. Diana Schneider, the ACET *ex officio* representative to the Division of Immigration Health Services (DIHS), provided a status report on the program to continue TB therapy for ICE detainees. DIHS implements the program by coordinating with state and local health departments, TB referral and tracking organizations, and national TB control programs. Several activities have been conducted since February 2002 to create the program, including development of ACET's recommendations and an *MMWR* article on continuity of TB therapy for ICE detainees; formation of a governmental workgroup and subgroups; ICE approval of the medical hold policy; and creation of a standard operating procedure (SOP), case scenarios and evaluation and monitoring criteria. Activities of the international workgroups are outlined below.

The Legal Issues Workgroup discussed strategies to engage the Border Patrol and sent a letter to the Undersecretary of the Border and Transportation Security Directorate requesting participation of U.S. Customs and Border Protection (CBP) in the workgroup. Immigration judges cannot be approached to become involved in this effort, but ICE has

decision-making authority to grant stays of removal for MDR-TB patients and other medically complex cases. However, stays of removal will be managed on a case-by-case basis. ICE will most likely attach conditions for detainees released into the community. For example, ICE would be notified if the detainee does not adhere to treatment or when therapy is completed. Detainees could legally remain in custody until treatment is completed, but this resource issue will be significant for ICE and responsible health jurisdictions. The workgroup began developing case scenarios to guide decisions on seeking stays of removal.

The Implementation Workgroup provided input on the DIHS SOP for medical holds, stays of removal, and coordination with CureTB, TBNet and the Binational TB Referral Project. The SOP was approved and distributed to the National TB Controllers Association (NTCA) for wider circulation to its membership. California has developed and approved an algorithm for its local health departments based on the DIHS SOP. ICE and DIHS drafted a memorandum to contract facilities requesting that ICE be notified of TB cases and suspects in custody. A copy of the memorandum was circulated to NTCA. TB controllers and NTCA also received a list of contract detention facilities and jails in each state. Program implementation also includes TB-positive persons being held by a county or state facility, U.S. Marshals or the Federal Bureau of Prisons who will be transferred to ICE custody after completing their sentences.

Collaborative efforts were undertaken with BHC to expand coordinated removals and the medical meet and greet program because DIHS is interested in broadening the Arizona model throughout Mexico and in other countries. The Mexico National TB Program has expressed interest in this initiative. A strategy was developed to communicate and disseminate information to states. The TB section of the draft DIHS *Infection Control Manual* was distributed to partners for review and input. DIHS has faced several challenges in implementing the workgroup's recommendations. Criteria to initiate treatment differ between the United States and receiving country. For example, Mexico will not treat unconfirmed TB cases. A process has not been developed to address non-adherence to treatment.

Stay of removal issues have not been resolved, such as the patient's residence while completing treatment and financial responsibility for therapy. ICE is only funded for health services during an average detention duration of ~30 days. Custody and changes in custody may produce clustering in certain states and local health jurisdictions. Detainees with TB may not be counted in national surveillance data or may be counted in other countries. Resource implications may occur from additional involvement of health departments in coordinating case management for post-custody care and an increase in the volume of enrollments in TB referral programs and tracking organizations. For example, TBNET forwards case information to any provider in the world before the detainee is deported.

The Evaluation and Monitoring Workgroup discussed routine monitoring versus one-time evaluation and the need for a clear dissemination plan. The workgroup is also developing monitoring criteria and a plan to collect and share data across programs. Goals are being established to identify successful and problem areas, develop interventions, establish or revise policies and impact change.

DIHS will take several actions to advance activities and respond to recommendations of the workgroups. Notifications of cases from contract facilities and jails will be reinforced. A protocol will be developed to monitor continuity of care in the overall program. DIHS policy regarding communication with local health departments will be strengthened. CBP, the Federal Bureau of Prisons and U.S. Marshals will be asked to participate on the workgroups. Public health laboratories will be asked to forward TB results directly to referral programs. DIHS will continue to give presentations of the initiative during meetings and workshops of organizations.

ACET commended Dr. Schneider's outstanding efforts in leading and organizing the project for a long period of time to ensure continuity of TB therapy for ICE detainees.

TB Control Efforts in U.S. Pacific Island Jurisdictions (PIJs)

Dr. Zachary Taylor of DTBE discussed CDC's TB control efforts in PIJs. CDC has responsibility for two territories, a commonwealth and three independent Compact of Free Association (COFA) nations. Under COFA, the United States can provide the three nations with aid and defense, exclude any other nation from having a military presence, and allow persons from COFA nations to enter and establish residency in the United States without a visa or legal immigrant status. The three COFA nations are the Federated States of Micronesia (FSM) with a population of 108,045; Republic of Marshall Islands (RMI) with a population of 57,471; and Palau with a population of 19,710.

In 2003, WHO estimated that both FSM and RMI had TB case rates of 87/100,000 with 94 cases from FSM and 50 cases from RMI. Palau had nine cases in 2003 with a case rate of ~46/100,000. TB cases from the COFA nations have impacted the United States. Most notably, Hawaii receives ~6,000 persons each year from COFA nations. From 1999-2003, 50 TB cases were reported and represented ~9% of foreign-born cases in Hawaii. The estimated population of 7,000 Marshallese in Arkansas is the highest in the United States. From 1993-2004, TB cases by sputum culture status among Marshallese in Arkansas gradually increased with 13 cases reported in this population in 2004 and a case rate of >100/100,000. Marshallese TB cases in Arkansas are younger persons with 30% <15 years of age who are less likely to be

sputum smear-positive, sputum culture-positive and HIV-positive. The Arkansas Department of Health is closely collaborating with the Marshallese community to overcome religious, cultural and other barriers to accessing this population.

HHS, WHO and the Secretariat of the Pacific Community (SPC) are the primary agencies that support TB control in U.S.-affiliated PIJs. The most significant challenges in addressing health needs in the COFA nations include a weak healthcare infrastructure; poor laboratory capacity; different program needs among the nations; large geographical areas within the nations requiring air travel; migration of persons to various jurisdictions; multiple agencies with different policies and strategies; and limited resources. CDC allocates ~$417,000 to the three COFA nations collectively.

DTBE has established several goals to strengthen TB control programs in PIJs and minimize disease transmission when citizens of COFA nations enter the U.S. mainland. Capacity of U.S.-affiliated PIJ TB control programs will be systematically developed and sustained to appropriately diagnose and treat TB suspects, cases and contacts. Efforts will be made to ensure resources are effectively used. Partnerships will be fostered among the jurisdictions to assure success of programmatic interventions. DTBE is guiding the achievement of these goals with a mission and philosophy to fully implement the WHO DOTS strategy with enhancements for TB control program development, program and staff capacity building, accountability of program activities, and ability to sustain initiatives.

DTBE implemented an approach to develop capacity in PIJs from 2002-2004. Intensive technical assistance (TA), training and TB laboratory infrastructure support were provided onsite or in remote areas. Shipping protocols were established for culture and susceptibility test results. The Pacific Island TB Controllers Association (PITCA) was formed and held an inaugural meeting in December 2003 with stakeholders to initiate the development of a laboratory improvement plan. PITCA's 2004 meeting focused on establishing goals for surveillance, evaluation and development of operating manuals. PITCA's 2005 meeting will address medical training, surveillance, cohort review and evaluation.

DTBE established several objectives for all U.S. PIJ TB programs to meet by December 2004. CDC funds would be utilized to support DOTS workers and laboratory technicians. Local acid-fast bacilli smear microscopy would be provided. Protocols would be developed and implemented to ship TB specimens to the California laboratory for culture and susceptibility testing. All of the objectives were accomplished and resulted in DTBE supporting shipping needs of other CIOs for measles, HIV and other diseases. DTBE established additional objectives for all U.S. PIJ TB programs to meet by December 2007. A standardized surveillance registry will be implemented. Reports will be submitted on progress toward meeting national or country-specific performance

measurements. Local program operations manuals will be developed that incorporate CDC and WHO protocols and address contact investigation. A program and laboratory evaluation plan will be implemented.

DTBE has created an approach to continue to develop capacity in PIJs from 2005 and thereafter. Intensive TA, support and training onsite or in remote areas will continue to be provided. Case management will be strengthened and national TB manuals will be developed. A comprehensive and accurate surveillance system will be implemented and voluntary HIV counseling and testing will be promoted. Household contact investigations will be initiated to prevent TB among children. Institutional infection control will be implemented.

To achieve these goals, DTBE will continue to coordinate activities with WHO and SPC, provide TB clinical training, increase awareness of health disparities, support regional networking and facilitate medical consultation. DTBE realizes that control of TB in PIJs is an important component of the domestic agenda and will continue to focus efforts in PIJs to promote and expand WHO DOTS strategies. TB program capacity development activities are ongoing, but new challenges will require additional interventions. Both DTBE and PIJ programs will need more resources to sustain activities.

Dr. Kawamura announced that the Hawaii Department of Health TB Control Program sent her a letter dated January 30, 2005 to express support of CDC's presentation and ACET's ongoing discussion of TB control in COFA nations. The letter was distributed in the meeting packets for the members to review. ACET was extremely impressed with the phenomenal efforts of CDC, WHO and SPC to systematically strengthen TB control, laboratory surveillance and treatment in PIJs. CDC and its key partners are conducting PITCA meetings and training activities in a culturally appropriate manner.

Discussion with the CCID Director

Dr. Mitchell Cohen formally introduced himself to ACET by describing his background and history at CDC. He then responded to ACET's questions as follows. One, CDC is aware that its efforts in succession planning must be strengthened to address current vacancies among senior leadership. For example, a recent study showed that 41% of NCID supervisors will be eligible for retirement within the next five years. CCID's highest priorities will be to maintain and build staff, continue to produce the best science and expand services. The Office of Workforce and Career Development will have responsibility for building both internal and external public health structures of the workforce by identifying training grants, fellowships and other new opportunities.

Two, Dr. Gerberding recently announced that she has no plans to resign as the CDC Director. The proposals she has presented to strengthen CDC's public health impact and enhance its prioritization of activities are extremely well supported throughout several branches of government, including the White House, Capitol Hill and HHS.

Three, one of CCID's primary roles will be to identify areas of synergy across programs. For example, HIV is a solid model to leverage resources for TB, but other respiratory diseases should be reviewed as well. Global health is an additional arena for an alliance with TB and TB may also serve as a solid programmatic model to track dollars and monitor impact under CDC's new organizational structure. However, CCID is aware of a significant threat to TB control and elimination. Successes in TB control efforts have resulted in perceptions throughout all levels of the government that resources do not need to be provided in this area. CCID will review concerns raised by ACET to identify mechanisms that can be created to resolve problems. For example, CCID can attempt to take advantage of relationships between TB and the increasing emphasis on pandemic influenza, severe acute respiratory syndrome (SARS) and other respiratory diseases to strengthen partnerships across different disease areas.

Four, CDC's new organizational structure with coordinating centers and additional offices will not affect funding to programs. CDC's new budget contains a leadership and management support line item that is a fixed level of funding. CDC will have access to $170 million that is separate from programmatic dollars. Program funds cannot be used for the leadership and management line item, but leadership and management dollars can be allocated to programs. This funding structure will provide an incentive to reduce rather than grow leadership and management costs and personnel.

Five, each coordinating center is responsible for establishing links with other programs. For example, both CCID and the Office of Global Health (OGC) receive funding to conduct international activities. The offices will make efforts to collaborate, identify needs and develop strategies to combine resources for implementation of global initiatives. Both CCID and OGC will be responsible for outcomes of joint global projects.

Six, CCID will partner with OSI on the management of goals. For example, OSI would assist CCID in adding TB to the health disparities list for minority populations and strengthening other advocacy efforts for TB. Under the goals management strategy, CCID and OSI would collect and assess data to identify priority areas, develop KPIs, leverage resources, and monitor, track and evolve activities. OSI will form and facilitate goals management teams for different issues, while coordinating centers will convene networks for overarching or cross-cutting areas. For example, CCID would establish networks for respiratory diseases, food- and waterborne diseases and healthcare safety. This process should lead to a prioritization of evidence-based activities.

Seven, ACET is on record with its position that bioterrorism resources should be used to enhance laboratory capacity, develop the workforce, and strengthen TB elimination and control efforts. However, the allocation of preparedness dollars continues to be a tremendous source of debate at both Congressional and HHS levels. On the one hand, preparedness funds should be dedicated; on the other hand, these dollars should be used to strengthen infrastructure by providing training and capacity building. CCID will play a role in determining and arguing CDC's position on this important issue. Eight, the new organizational structure will place more emphasis on increasing, better defining and leveraging additional resources for extramural activities by obtaining broad input on CDC's role in public health research.

On behalf of ACET, Dr. Kawamura accepted Dr. Cohen's offer to schedule "CCID discussions" as a regular item on future meeting agendas. The discussions will provide ACET with an opportunity to describe issues that should be brought to the attention of CDC leadership. ACET strongly emphasized the need for CCID to adequately fund and support TBTC projects, particularly with the expansion of global TB initiatives. GATDD's goals to shorten TB therapy cannot be achieved without critical research by TBTC, such as the moxifloxacin trial. ACET requested that CCID serve as an internal advocate within CDC to assist in building the TB budget. For example, CCID could request that Dr. Gerberding or other CDC senior leaders use existing flexibility or authority to transfer dollars to the tremendously underfunded area of TB.

With no further discussion or business brought before ACET, Dr. Kawamura recessed the meeting at 5:00 p.m. on February 16, 2005.

Current ACET Business

Dr. Kawamura reconvened the meeting at 8:30 a.m. on February 17, 2005 and entertained a motion to accept the previous meeting minutes. The motion was properly made and seconded by voting members. The October 6-7, 2004 ACET Meeting Minutes were unanimously approved with no changes or further discussion.

Dr. Valdiserri announced that the *Federal Register* notice of CDC's four public meetings to obtain input on its agency-wide research agenda was distributed to ACET for review. The meetings will be held on March 8, 2005 in Arlington, Virginia; March 18, 2005 in Atlanta, Georgia; March 24, 2005 in Seattle, Washington; and March 31, 2005 in Columbus, Ohio. The public is invited to attend the meetings so long as persons register in advance and space is available. CDC is requesting that ACET be represented at one or more of the meetings and Dr. Kawamura will receive an official invitation to attend one of the meetings to represent ACET.

Update on the Respiratory Protection for Airborne Infectious Agents Stakeholders' Workshop

Dr. Adelisa Panlilio, of the CDC Division of Healthcare Quality Promotion, described the key outcomes of the meeting. The workshop was held on November 30-December 1, 2004 in Atlanta with three major objectives. The current scientific knowledge of transmission of selected airborne infectious agents (AIAs) and respiratory protection for AIAs was discussed. Strategies to improve the quality of respiratory protection were explored. Critical research and "policy" needs were identified and a time-line was developed to address these needs.

The workshop was organized into five plenary and three breakout sessions with a diverse group of participants assigned to each breakout session. Question and answer periods were provided throughout the workshop to allow stakeholders to engage in dialogue with presenters. The five plenary sessions covered the basics of AIA control; current state of knowledge about TB, SARS, influenza and smallpox; current state-of-science about respiratory protection; research on respirator performance; and regulatory perspectives and outlooks. The three breakout sessions allowed participants to address the five plenary session topics in more detail and discuss outlooks from manufacturers and users. The workshop concluded with summaries of the breakout sessions by CDC moderators and an overview of the meeting by Dr. Dixie Snider, Director of the CDC Office of Chief of Science.

The workshop resulted in several key recommendations to CDC from the participants. The current evidence base should be used to inform the development of guidelines of respiratory protection for AIAs. CDC and external partners should jointly create a research agenda on respiratory protection for AIAs. The research agenda should cover diagnostics for rapid risk assessment of AIAs, behavioral science, and effective interventions that prevent transmission and provide respiratory protection.

CDC will attempt to respond to the participants' recommendations with the following actions. New knowledge from research will be used to improve guidelines, interventions and health outcomes. Internal CDC clearance of documents that address respiratory protection and infection control will be better coordinated. CDC documents that address infection control of AIAs will be harmonized. For example, Associate Directors for Science in the respective CIOs have initiated discussions to coordinate CDC's TB, smallpox and isolation guidelines to ensure consistency among the documents. A report of the overall workshop, breakout session summaries and slide presentations will be cleared by CDC and then posted on the web site of the National Institute for Occupational Safety and Health (NIOSH).

Several ACET members attended the workshop and provided their perspectives. The workshop served as a valuable opportunity to engage in dialogue, particularly since diverse groups identified areas of disagreement, gaps and research needs. The workshop also provided a forum to outline unanswered questions and identify areas of agreement in respiratory protection. For example, all participants recognized the critical importance of source control and union representatives agreed that respiratory protection should be provided to workers. The workshop should provide CDC with a solid foundation to advance the development of evidence-based guidelines on respiratory protection of AIAs.

Other ACET members were uncertain of the impact of the workshop because several groups continue to debate the issue and have not changed positions about fit testing over the last decade. Manufacturers are primarily motivated by the business aspects of selling respirators and conducting fit testing, but are also concerned about liability issues that may require national legislation. Clinicians are more interested in the practical aspects of the evidence base for annual fit testing. Annual fit testing was the most contentious source of disagreement during the workshop because the requirement is based on industrial data rather than evidence about infectious aerosols. Neither NIOSH nor the Occupational Safety and Health Administration (OSHA) expressed any flexibility from a regulatory perspective in developing respiratory protection standards.

ACET members and OSHA representatives had a discussion prior to the workshop. Representatives of OSHA stated its intent to take the lead from CDC due to current disagreements within CDC about respiratory protection. However, OSHA cannot change its current recommendations without strong guidance from CDC. Overall, the workshop did not serve as a forum to resolve various positions of different groups; gain new knowledge about the dynamics of TB infection and transmission; discuss research on the dissemination of organisms among patients; or describe strategies to more effectively measure health outcomes and utilize resources. For example, more emphasis was placed on personal protective equipment (PPE) issues during the workshop than risk analysis. The participants were not offered guidance on actions to take now with regard to fit testing while CDC is attempting to develop a respiratory protection research agenda.

Several ACET members also noted that CDC has not provided sufficient leadership over the past ten years to concede differences in opinion and resolve the fit testing debate from both environmental and epidemiological perspectives. The current debate is disturbing because the development of a respiratory protection research agenda will continue to be delayed unless CDC takes a strong leadership role. Minimal progress has been made since the original respiratory protection research agenda was proposed ten years ago.

CDC agreed with several of ACET's observations. Controversial issues and perspectives of the various disciplines were not resolved during the workshop, but concerns about SARS and smallpox are driving CDC to devote resources to the development of a respiratory protection research agenda. Most notably, CDC is sponsoring a series of studies on infection control interventions in Brazil, Peru, Russia and other countries. Qualitative and quantitative fit-test results and other health outcome data from this research are currently being analyzed and will be presented to ACET during a future meeting. CDC will use the new findings to change policy and hopes to incorporate a respirator component into the research as future QFT studies are developed in the United States and other countries.

CDC and USAID are funding projects in South Africa to replicate the Riley guinea pig experiments. The NIOSH National Personal Protective Technology Laboratory is currently implementing recommendations from the workshop to develop a blueprint that will guide the establishment of a research program. This effort may generate data in response to several questions raised during the workshop. CDC is in the process of establishing a laboratory at Fort Dietrich that will be dedicated to research on microbiology and airborne transmission of infectious diseases.

Overall, CDC agreed with ACET that advances will not be made in respiratory protection without strong leadership and dedicated funding. Resources must be allocated for CDC to sponsor solid respiratory protection research, particularly since current guidance is based on differing expert opinions. ACET was advised to communicate with Dr. Snider if consensus is reached to make a statement about CDC's next steps in answering questions to inform the development of respiratory protection guidelines and creating a research agenda. ACET can also invite Dr. Snider to attend the next meeting or request that he meet with a small group of members prior to the next meeting.

ACET made several suggestions to conclude the discussion. CCID could take a lead role in coordinating the development of a respiratory protection research agenda within CDC. The possibility should be explored for TBESC or TBTC to undertake this research. ACET should formalize a statement to encourage leadership at the level of the CDC Director to make a decision on developing interim respiratory protection guidelines for annual fit testing. ACET's statement should advocate for prioritization of a respiratory protection research agenda in the CDC-wide research agenda, including health outcome studies on the utility of annual fit testing. ACET tabled formal actions on the suggestions until after the next presentation.

Update on the Revised Infection Control Guidelines

Dr. Michael Iademarco of DTBE provided a status report on CDC's recent activities to revise the draft guidelines. Comments from ACET and the Healthcare Infection Control Practices Advisory Committee were addressed. The public comment period was announced in the *Federal Register* on December 6, 2004 and the docket closed on February 4, 2005. CDC is currently addressing the public comments and will conduct a formative evaluation to determine usability of the comments. The need for CDC to re-clear the guidelines will be assessed based on the magnitude of revisions. The final document will be published in the *MMWR* and educational materials will be developed.

The 123 submissions of both individual and group comments included federal agencies, unions, private organizations and manufacturers. Of ~2,000 category-specific comments, the majority have been entered in a database that will be used to track and respond to comments. The most significant concerns raised about the guidelines are as follows. Tuberculin skin testing (TST) training is unrealistic. As a result, CDC will add National Health And Nutrition Examination Survey methods as a model plan.

The option for visitors to wear respirators and the recommendation for HCWs to wear respirators between settings and in vehicles while transporting patients based on a risk assessment are problematic. The guidelines are too long; the frequency of fit testing is an issue; and the reference to OSHA's annual fit-testing regulations is a significant obstacle that needs to be resolved. CDC is considering the possibility of simply stating that "OSHA regulations are available" and providing a link to the document.

Comments were submitted to support both sides of the fit-testing argument, including annual training, initial and periodic fit testing, insufficient data to make recommendations on the frequency of fit testing, the usefulness of fit testing as an adjunct in training, and the need for fit testing to guide changes in the face or respirator. The public identified two major gaps in the draft guidelines related to the transition from QFT to QFT-Gold as well as serial screening and movement of HCWs among different settings and the potential for various risks. No substantial comments were submitted to support a change in CDC's initial and periodic fit testing recommendation.

ACET commended DTBE for its diligent efforts over a long period of time in revising the guidelines and taking tremendous steps to broadly obtain public comments. However, some members expressed concerns about the current draft and the overall process. The guidelines serve as a body of recommendations and should not mention OSHA's annual fit-testing regulations at all. A strong possibility exists for a link to OSHA to be misinterpreted as a regulation.

The current document demonstrates that DTBE obviously did not act on ACET's previous recommendations and comments by other organizations and does not intend to change guidelines cross-cleared by various CDC CIOs. For example, ACET and other groups expressed concerns about CDC's recommendation for initial and periodic fit testing. DTBE has yet to act on ACET's previous request to provide evidence to support the necessity of periodic fit testing. This situation is extremely discouraging to the many groups and individuals who made diligent efforts in evaluating and responding to the document.

ACET concluded the discussion with general agreement to send a letter to Dr. Snider to discuss the revised infection control guidelines since the document must be cross-cleared by the Office of the Director and other levels above DTBE. ACET will also use the letter to raise outstanding issues about the stakeholders' workshop and ask questions about CDC's next steps in developing a respiratory research agenda. Key points that will be emphasized in the letter are described below.

- Dr. Snider will be thanked for his leadership in crafting the agenda for the stakeholders' workers and listening to ACET's concerns. He will be invited to attend the next ACET meeting and will also be asked to meet with a smaller group of members prior to the next meeting if his schedule permits.
- Health outcome studies regarding the utility of annual fit testing will be encouraged.
- The importance of a cohesive CDC policy that includes all components of CDC will be acknowledged.
- The critical need to use the best available evidence to define and promulgate information on infection control and respiratory protection will be underscored.
- Deletion of the reference to OSHA regulations in the infection control guidelines will be encouraged because the text weakens the position of the document as the gold standard for HCWs.
- A recommendation will be made for CDC to leverage adequate funding of a research agenda that covers three topics in the following order of importance: outcome research to define the relevant importance of the hierarchy of controls; data on the use and frequency of testing respirators, masks and other PPE; and evidence on differences in disease causation for various infectious and non-infectious aerosolized particles.
- The importance of CDC guidance will be emphasized. The FY'05 Labor House bill explicitly prohibits OSHA from administering or enforcing the general industry respiratory protection standard for annual fit testing for occupational exposure to TB. The conference report language states that the conferees concurred with the House bill and report language regarding

OSHA's enforcement of the respiratory standard applied to TB. The conferees advised OSHA to take no further action with regard to respiratory protection for occupational exposure to TB until such time as CDC completes its ongoing revision of the TB guideline.

Dr. Kawamura will electronically distribute a draft of the letter to Dr. Snider to ACET for review and a formal vote.

TB and MDR-TB Among U.S.-Bound Hmong Refugees

Dr. Susan Maloney of DGMQ described CDC's continued efforts to address TB in foreign-born populations. The proportion of U.S. TB cases among foreign-born persons is now >53% of the population. Hmong refugees fled to Thailand from Laos ~20 years ago due to a history of persecution and first began resettling in the United States ~10 years ago. In 2004, CDC was notified about residents of Wat Tham Krabok near Bangkok and the Thai government urged U.S. resettlement of ~15,000 refugees. CDC anticipated high TB rates in this population due to limited access to health care and 52% of these persons are <15 years of age.

From March 2004-January 2005, standard overseas TB screening of Hmong refugees was initiated and CDC's #1 enhanced TB screening recommendations were implemented. The movement of Hmong refugees was halted because 27 cases of MDR-TB and active TB were detected overseas and in the United States. Investigations were launched overseas and in the United States with CDC's #2 enhanced TB screening recommendations. Of 15,645 Hmong refugees, 9,455 have arrived in the United States and 6,190 are still in Thailand. The majority of adults in the United States underwent initial overseas screening with standard or CDC's #1 enhanced TB screening recommendations. A chart of the standard and CDC's #1 and #2 enhanced TB screening recommendations was distributed to ACET for review.

Of ~424 refugees in Thailand with overseas TB classifications, ~351 had TB cultures performed. Of those, 56 had positive TB culture results, 184 had negative results and 111 are pending. Of the 56 TB-positive cases, 17 have MDR-TB. Preliminary data of Hmong refugees show that 175 of 247 active TB cases in Thailand are on treatment. Among adults, CDC estimates extremely high rates of 3,294/100,000 of active TB and 227/100,000 of MDR-TB. Of the 17 MDR-TB cases in Thailand, the median age is 37 years, 10 cases are among males, one has HIV co-infection, six have cavitary disease or prior TB treatment, six report TB signs and symptoms, and nine are smear-negative.

CDC is currently developing treatment recommendations for the MDR-TB cases and is also creating guidelines for contacts of both active TB and MDR-TB cases that will be

disseminated to states. DTBE will deploy an MDR-TB expert to Thailand to provide training and establish a program. A CDC mission in Thailand with TB expertise will oversee MDR-TB treatment as well. CDC deployed a six-member team of epidemiologists, clinicians and laboratorians to Thailand to investigate the epidemiology of TB among Hmong refugees; implement appropriate control measures; evaluate TB screening and treatment algorithms; and provide recommendations on TB diagnosis and treatment.

The U.S.-based investigation of newly arrived Hmong refugees is designed to systematically identify active TB cases, develop guidance for and measure outcomes of stateside evaluations, and evaluate the quality and performance of overseas TB screening algorithms. Of 27 states where 8,826 Hmong refugees have resettled, Minnesota, California, Wisconsin, Michigan and North Carolina represent the top five. Preliminary data from state case counts show that 30 TB cases were verified in resettled Hmong refugees as of February 10, 2005. Of those, three were MDR-TB cases.

CDC has estimated that treatment costs of Hmong refugees will range from $1,000-$60,000 for active TB and $90,000-$1 million for MDR-TB. Long-term programmatic issues related to LTBI will need to be addressed as well. CDC is formulating recommendations for evaluation and treatment of LTBI cases among Hmong refugees in the United States and will also partner with providers and voluntary organizations that serve the Hmong community to develop an outreach program. These efforts will be designed to ensure Hmong refugees are provided with information to access health care.

CDC is facing other barriers to TB evaluation and treatment in Hmong refugees in addition to cost, such as limitations of overseas TB screening and treatment programs; a lengthy time period between the overseas examination and approval of U.S. arrival; challenges for stateside notification and follow-up; lack of standardized initial stateside refugee health evaluations; lack of public health resources; and unresolved issues related to health insurance coverage for refugees.

ACET emphasized the critical need for CDC to immediately strengthen overseas TB screening and stateside refugee health examinations for all populations. Previous experience has shown that other refugee groups were smear-positive upon U.S. entry. ACET was also concerned that CDC's efforts to address LTBI in Hmong refugees in the United States do not include plans to identify and re-screen persons. CDC's education and outreach activities will not be sufficient to detect additional cases of TB and MDR-TB that Hmong refugees will spread in communities throughout the United States. ACET underscored the critical importance of DOS providing resources to states to respond to the public health impact from this new and overwhelming TB burden. ACET

raised the possibility of revising the current policy to treat patients who are found to be smear-negative and culture-positive with active pulmonary TB during the screening process.

A motion was properly placed on the floor by a voting member to adopt ACET's February 11, 2005 draft letter to the HHS Secretary. The letter contains three recommendations in response to the resettlement of Hmong refugees in the United States. First, a waiver should be granted to the requirement that refugee health funds from the HHS Office of Refugee Resettlement be utilized within the first 90 days of arrival for completion of health screening. Second, the eligibility period for federal refugee medical assistance should be extended until TB infection or disease is fully treated for a refugee. Third, federal funding should be augmented to heavily impacted states to hire state and local public health staff to manage and implement this effort.

The motion was properly seconded by a voting member, but several suggestions were made before a vote was called. First, the letter should be expanded to emphasize the extra burden of Hmong refugees on TB laboratory testing resources. Text should be added on page one to request additional resources for laboratories to detect TB in this population and provide drug susceptibility testing to guide treatment. A new recommendation should be included on page two to supplement funding to provide critical TB laboratory testing. Second, the letter should be revised to be more generic for new refugee groups that will enter the United States in the future.

Third, a new recommendation should be added to page two to prioritize the evaluation and probable revision of the overseas medical screening and stateside follow-up processes. Fourth, a new recommendation should be incorporated on page two to request adequate resources to identify and treat TB in Hmong refugees in Thailand. Fifth, the majority of the background information should be deleted. The letter should be short, concise and focused on ACET's recommendations to the HHS Secretary.

ACET **unanimously approved** the Hmong refugee letter to the HHS Secretary with a modification to incorporate language on the need for additional laboratory resources. The letter will be electronically distributed to ACET for review. Dr. Kawamura will request a meeting with the HHS Secretary to discuss the situation with Hmong refugees and outline other priority issues on ACET's current agenda.

Public Comment Period

The Chair opened the floor for public comments; no attendees responded.

New ACET Business

ACET proposed the following topics to add to the ongoing list of agenda items.

- ACET discussion and recommendations to CDC on the QFT-Gold guidelines in support of a "TB diagnostics" meeting theme. **[June 2005 meeting]**
- Status report by DTBE on actions taken to address the ACET Foreign-Born Workgroup recommendations.
- Status report by Dr. Charles Schable, the Office of Terrorism Preparedness and Emergency Response Director, on CDC's actions to address ACET's recommendation to define full use of emergency preparedness funding.
- Update by NCHSTP on outcomes of CDC's four public meetings to obtain input on its agency-wide research agenda.
- Update on the Surgeon General's Call for Action regarding global TB and health disparities.
- Presentation by Dr. Garth Graham of HHS on progress made to include TB on the health disparities list for minorities. ACET will provide Dr. Graham with its letter to Admiral Richard Walling in preparation of the presentation. **[June 2005 meeting]**

Dr. Kawamura opened the floor for ACET to comment on previous agenda items. In terms of the draft QFT-Gold guidelines, DTBE expects to produce the document by March 16, 2005 and hopes to electronically distribute a working draft to ACET for review and comment prior to this time. DTBE will not recommend use of QFT-Gold in a manner that is inconsistent with targeted screening and treatment of persons with LTBI. HCWs in screening programs will be the exception to this guidance, but data are currently insufficient for DTBE to make recommendations on the use of QFT-Gold in pediatric populations, HIV-positive persons and TB contacts.

ACET strongly emphasized the need for the QFT-Gold guidelines to clarify that clinical decisions about active TB disease should never be made on the basis of QFT or TST results. Restrictions on the use of QFT-Gold will hamper wide use of the test in the future. A wealth of information can be obtained if QFT-Gold is allowed to be used in an unrestricted manner. ACET endorsed DTBE's novel approach of offering guidance to interpret QFT-Gold results rather than providing recommendations on the appropriate time and situation to use the test. This strategy will assist in resolving reimbursement issues. CDC confirmed that ACET's concerns will be considered during the ongoing development of the QFT-Gold guidelines, particularly reimbursement issues and unintended restrictions of using the test.

With respect to CDC's global TB activities, ACET pointed out that several undeveloped countries do not produce outcome data on national TB isolation policies. DTBE was asked to facilitate efforts in strengthening this area. Overall, ACET commended DTBE's remarkable leadership, technical assistance and other efforts in global TB control, particularly since CDC does not receive funding for these initiatives. However, ACET reiterated its previous suggestion for DTBE to more strongly emphasize Mexico because the country has a tremendous impact on domestic TB control efforts. Screening of immigrants from Asia and other "hot spot" countries should also be prioritized. ACET is hopeful that DTBE's foreign-born guidelines will significantly contribute to these improvements.

CDC's position is that advances will be made in global TB because OGC is also focusing on priorities for global disease detection, particularly for emerging and reemerging diseases. Moreover, MDR-TB in Hmong refugees may provide an opportunity to use Congressional funding allocated to CDC specifically for emerging and reemerging global diseases. This synergy may also allow DTBE to enhance communication and coordination with OGC. ACET raised the possibility of asking CCID to list TB as a disease to enhance bioterrorism information systems. DTBE confirmed that it will follow up with OGC to discuss global laboratory capacity focusing on Asia and rapid information systems to benefit notification of TB and other diseases.

Closing Session

The date of the June 2005 ACET meeting was not scheduled due to several conflicts with other conferences during the month. DTBE will poll the members by e-mail to suggest and confirm the next meeting date.

With no further discussion or business brought before ACET, Dr. Kawamura adjourned the meeting at 11:36 a.m. on February 17, 2005.

I hereby certify that to the best of my knowledge, the foregoing Minutes of the proceedings are accurate and complete.

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Date

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L. Masae Kawamura, M.D.
ACET Chair